by 10.7% and 11.4%, respectively; CaT80 and CaT50 reduced by 6% and 5.3%, respectively). During maintained stretch, a gradual re-lengthening of APD and CaT duration was observed. After release of stretch, APD and CaT duration reverted to shorter values.
Conclusion: Living cardiac tissue slices offer a promising experimental model for the study of cardiac mechano-electric coupling. The methodology described can be refined (e.g. using a computer-controlled motorised stage to synchronise electrical and mechanical events, and by use of fiducial markers to track local tissue deformation rather than only input strain levels) and extended (e.g. exploring effects of stretch directionality, relative to prevailing cell orientation in a slice).

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Dual Spikes of Catecholamine Releases from Sympathetic Nerves in Rodent Heart Slices Following Hypoxia-Reperfusion as Recorded by a Novel Electrochemical Method
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Sympathetic nerve in heart is essential in cardiac physiology and diseases, because it releases catecholamines to regulate cardiac cells including ventricular myocytes, atrial myocytes and vas through GPCRs. With a modified glass-insulated micro carbon fiber electrode (pegCFE), we record stimulus (depolarization or hypoxia)-signals via either amperometric current (I_{amp}) or fast cyclic voltammetry from the nerve terminals in rodent hearts, by a method termed cardiac Slice of ElectroChemistry (cSEC). We found that, (1) cSEC signal I_{amp} is dependent on CFE-voltage and extracellular Ca^{2+}; (2) pharmacologically, I_{amp} is increased 40% by Yohimbine, and decreased 60% by reserpine; (3) electronic microscope detected dese core vesicles, tyrosine hydroxylase (TH) immunostaining and TH-GFP transgenic mice showed massive TH-signal in whole heart; (4) as determined by in-situ FCV, as well as microdialysis-based HPLC, NE and/or DHPG (a NE metabolic substance) were responsible for cSEC signals. These evidences establish that the evoked cSEC signals represent catecholamine releases from sympathetic nerves in heart slices. Using cSEC we discovered that hypoxia-reperfusion triggered dual spikes of catecholamine release at pH 7.4: first peak at 10s following hypoxia perfusion, second peak at 10s following normoxia perfusion. Finally, catecholamine release were reduced by 75% in ventricle slices from syt7(Ca^{2+} sensor)-KO versus WT mice, indicating cSEC may serve phenotyping of any sympathetic defects in cardiac disease animal models.
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Electronic Expression of IK1 in Human Induced Pluripotent Stem Cell Derived Cardiocytes Reveals Atrial vs Ventricular Specific Properties
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Cardiomyocytes derived from human induced pluripotent stem cells (hIPSC-CMs) provide a promising platform for understanding human cardiac pathology and physiology. HIPSC-CMs differentiate into a mixed population of cells composed of ventricular, atrial, and nodal cell types; cellular phenotype is generally distinguished by morphology of the action potential (APs). However, in hIPSC-CMs a very small inward rectifying potassium channel (IK1) relative to native cardiac cells causes a depolarized membrane potential which contributes to inconsistent AP properties and misidentification of cellular phenotype. We used Electronic expression of IK1 via dynamic clamp to restore the AP and resting membrane potential back to a physiological levels. This allowed for improved discrimination of atrial and ventricular cells based on AP morphology. Using standard patch clamp techniques, we compared the inward sodium currents (INa) of cells with atrial and ventricular AP morphologies. INa current densities in cells with atrial like APs were larger than ventricular-like APs (at −30 mV, in pA/pF: −71.22 ± 6.96 (n=5) vs. −46.25 ±5.03 (n=14), $p < 0.05$). Analysis of steady-state inactivation parameters of INa showed that cells with an atrial like AP had a more negative steady-state inactivation (V1/2: −81.84 ± 2.75 (n=5) vs. −74.72 ±0.8 (n=14), $p<0.05$). Cells with atrial APs had a larger Kv1.5-like component at +50 mV than ventricular APs (in pA/pF: 3.71 ± 0.55 (n=5) vs 1.00 ± 0.10 (n=16),$P<0.05$) but similar peak currents: (6.89 ± 0.50 (n=5) vs. 6.58 ± 0 .67 (n=14),P=N.S). IK1 current density was more than 3x smaller in cells with atrial-like APs at −120 mV (in pA/pF: −0.71 ± 0.08 (n=5) vs. −3.45 ± 0.61 (n=14), $p<0.05$). These data suggest that differential AP morphology in hIPSC-CM has a similar electrophysiological basis to native cells.

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Normalization of Action Potential Properties in Human Induced Pluripotent Stem Cell Derived Cardiocytes by Electronic Expression of IK1
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Cardiac myocytes derived from human induced pluripotent stem cells (hiPSC-CMs) are a useful and renewable human myocyte model. Despite their promise, these cells have unexplored limitations when applied to action potential (AP) analysis. APs occur spontaneously and are associated with variability due to a small/missing inwardly rectifying potassium channel (IK1). We used whole cell voltage clamp with dynamic clamp to express IK1, which significantly improved the physiological behavior of the AP and electrical profile of hiPSC-CMs.
hiPSC-CMs have a negligible peak IK1 at −120 mV (−0.81 ± 0.4 pA/pF) which results in depolarized resting membrane potentials (RMP) (−60.0 ± 1.7 mV, n=17). ''Electronic transfection'' of IK1 into hiPSC-CMs results in re-establishing a physiological RMP (−84.0 ± 0.2 mV), increases the maximal upstroke velocity (from 82.1 ± 2.4 to 161.6 ± 11.5 mV/ms), reduces AP duration, and increases the rate of repolarization (from 0.35 ± 0.03 to 1.1 ± 0.1 mV/ms, n=17). Despite a detectable transient outward potassium current in hiPSC-CMs, ''spike and dome'' morphology is generally absent in spontaneously active cells; addition of electronic IK1 restored this morphology in 12 out of 17 ventricular cells. It also restored the relationship between maximum upstroke velocity and sodium current density. The stabilized membrane potential allowed systematic measurement of dynamic parameters. The rate dependence of the AP duration was measured in at different pacing rates from 4000 to 500 ms in 12 electronic IK1 expressing hiPSC-CMs and showed a classical monotonic restitution curve, with AP increasing with increased cycle length. By removing sodium channel inactivation, electronic expression of IK1 improves hiPSC-CMs utility in assess mechanisms involving sodium channels and phase 1 repolarization such as LQT3 and Brugada Syndrome.

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Activation of Ca^{2+}-Dependent Cation Current by Fluid Shear Force in Atrial Myocytes
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Atrial myocytes are subjected to fluid shear force (FSF) during each contraction and relaxation. Ionic currents regulated by shear force and their molecular integrity in cardiac myocytes have not been well-understood. We examined whether FSF activates specific current in atrial myocytes and underlying mechanisms for FSF-sensitive ionic current using whole-cell patch-clamp technique. A FSF of ~16 dyne/cm^2 was applied to entire single atrial myocyte using automated micro-puffing apparatus. A FSF-sensitive current (I_{FSF}) was detected in lowly Ca^{2+}-buffered (0.5 mM EGTA) atrial myocytes, but not in highly Ca^{2+}-buffered ($\geq$4 mM EGTA or 10 mM BAPTA) myocytes. The I_{FSF} showed an outward rectification with a reversal potential of about -6 mV. The I_{FSF} was inhibited by high concentrations (20-50 μM) of ryanodine and by replacement of external and internal cation with impermeant $NMDG^+$, suggesting that I_{FSF} is a Ca^{2+} release-dependent cation current. Application of either transient receptor potential melastatin subfamily 4 (TRPM4) inhibitor 9-phenanthrol or TRPM4-specific antibodies removed most of inward I_{FSF} and ~80% of outward I_{FSF}. However, stretch-activated cation channel blocker GsMTx-4 did not affect I_{FSF}. Interestingly, I_{FSF} was strongly inhibited by inositol 1,4,5-trisphosphate receptor (IP_3R) blockers, 2-APB (2 μM) or xestospongin C. In addition, in atrial myocytes isolated from type 2 IP_3R (IP_3R2) knock-out mouse, I_{FSF} was not detected, although 9-phenanthrol-sensitive I_{FSF} was recorded in wild-type myocytes. Co-immunostaining of TRPM4 and IP_3R2 in rat atrial myocytes revealed peripheral localization of these proteins with some co-localizations. These results suggest that fluid shear stimuli may activate TRPM4 channels in atrial myocytes via Ca^{2+} releases triggered by the activation of nearby IP_3R2.

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STIM1 Increases Ca^{2+} Stores in the Sarcoplasmic Reticulum of Adult Feline Ventricular Myocytes
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STIM1 is a Sarcoplasmic Reticulum (SR) membrane resident protein implicated in sensing and maintaining SR Ca^{2+} levels. The role of STIM1 in the regulation